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Reopening schools safely in the face of COVID-19: Can cluster randomized trials help?

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Abstract

The COVID-19 pandemic has highlighted the challenges of evidence-based health policymaking, as critical precautionary decisions, such as school closures, had to be made urgently on the basis of little evidence. As primary and secondary schools once again close in the face of surging infections, there is an opportunity to rigorously study their reopening. School-aged children appear to be less affected by COVID-19 than adults, yet schools may drive community transmission of the virus. Given the impact of school closures on both education and the economy, schools cannot remain closed indefinitely. But when and how can they be reopened safely? We argue that a cluster randomized trial is a rigorous and ethical way to resolve these uncertainties. We discuss key scientific, ethical, and resource considerations both to inform trial design of school reopenings and to prompt discussion of the merits and feasibility of conducting such a trial.

Keywords

COVID-19, public health, schools, cluster randomized trial, design, research ethics, informed consent

Introduction

The rapid onslaught of the COVID-19 pandemic meant that many public health policies had to be rapidly implemented despite substantial uncertainty about both the risks from SARS-CoV-2 and the effectiveness of various prevention measures. Although many governments have eased restrictions compared to where they started in the early days of the pandemic, surging numbers of infections have resulted in renewed limits on public activity, including additional rounds of school closures.[1] When numbers begin to improve again and governments renew steps toward reopening, there will be an opportunity to rigorously study the de-implementation of these policies and answer questions about the impact of closures on transmission of the virus, as well as when and how these restrictions can be safely lifted.[2] Although the concept of evidence-based policymaking has not yet become an expectation along the lines of evidence-based medicine, it is essential for policymakers to take advantage of this opportunity.[3]

Policy decisions about when and how to reopen primary and secondary schools are of particular social importance. In addition to allowing parents to return to work, reopening schools is essential to minimizing long-term consequences for children's education and development.[4] However, reopening may pose additional risks for the adults working in schools, the family members of children attending school, and community members coming into contact with any of these individuals. Reopening may also influence transmission rates indirectly, for example, by changing risk perception, leading to an increase in social activities outside of school, and by increasing parental exposures as they resume their own activities.[1] Although children appear to be substantially less affected by COVID-19 than adults, rare but serious effects following pediatric

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infection have been reported.[5] The role of children in transmission of the virus is also unsettled.[1,6–12]

There have been promising early reports regarding effective vaccine candidates for SARS-CoV-2, but supply and distribution challenges, as well as the need for further study in pediatric trials, mean that vaccines are unlikely to be able to support school reopening for some time.[13] Until an effective vaccine is available, evidence is required to prudently guide school reopening and closure decisions. We argue that the cluster randomized trial (CRT) is the most rigorous way of generating that evidence.[14,15] In what follows, we discuss key scientific, ethical, and resource considerations both to inform trial design of school reopenings and to prompt discussion of the merits and feasibility of conducting such a trial.

The need for a randomized trial

The driving factor for any randomized trial is the need to generate rigorous evidence. School reopening policies currently lack a rigorous evidence base, and this has led to wide variation in policies across the world. Taking Europe as an example: schools in Sweden remained open for children under 16 years throughout the pandemic; Denmark, Germany, and Norway reopened schools after a period of closure; and Italy and Spain elected to keep schools closed until fall.[16] Schools in Austria, the Czech Republic, and Russia have recently closed.[1] Variability is also seen within the United States at the state and county level. Many school districts partially reopened after extended closures, often on "hybrid models" with only a subset of students in school buildings each day while the remainder learns remotely. However, as cases surged several weeks into the fall term, plans to resume in-person learning have been delayed in some districts, while another round of closures has begun in others.[17–21] The justifications for these decisions also vary, with some officials relying on local test positivity rates (each with different thresholds for closure) and others focusing on numbers of new cases within schools.[1]

The currently available evidence on school closure and reopening is observational. For example, reopening primary schools in Quebec, Canada, was associated with relatively few new cases.[22,23] Yet, in Israel, opening primary and secondary schools were associated with several outbreaks and the reclosure of some schools.[24] More recently, schools in Georgia state in the United States reopened only to see dozens of cases and hundreds of students and staff quarantined within the first week.[25] However, given the observational nature of these data, whether these outbreaks were the result of school reopening or ongoing community transmission remains unclear. Moreover, it is difficult to draw conclusions from the many localities that moved to successfully reopen at the start of the school year when infection rates were down, given the widespread resurgence of the virus to even higher levels than earlier in the year. A randomized design is a rigorous way of determining the causal impact of school reopening on transmission rates.[26] This approach also avoids confounding based on different local approaches to avoiding community spread beyond school closures such as business closures and restrictions on social gatherings.

Study question and outcomes

School closures are generally motivated by desires to reduce community transmission of the virus (as seen in prior influenza epidemics)[27], beyond protecting those attending and working at schools. Therefore, the most pressing research question is: "Does reopening schools increase community transmission rates of SARS-CoV-2?" Accordingly, the primary outcome measure for a rigorous evaluation of reopening policies should be the incidence of SARS-CoV-2 in the wider community.

Secondary outcome measures should address the range of potential benefits and harms of school reopening policies. Categories of secondary outcomes include economic, educational, and socialization outcomes. Economic outcomes may include household income, hours of employment for parents, and reliance on paid child care. The full impact on child education and socialization is difficult to measure,[28] but relevant outcomes could include student performance in courses and standardized tests, as well as measures of child wellbeing, time spent interacting with peers, anxiety, depression, and aggression.[29] Particular attention should be paid to the impact on vulnerable students (e.g. those from lower socioeconomic backgrounds and those with different learning needs) as pre-specified sub-groups. Secondary outcomes might be obtained from routinely collected data, purposively collected regional surveys, or school-based assessments.

Cluster randomized design

Because public health policies typically target entire populations, the traditional randomized trial—which allocates individuals across intervention arms—is often not the appropriate experimental design. By contrast, CRTs are well suited to the rigorous evaluation of public health policies. CRTs randomize intact social units, such as geographic regions, municipalities, or schools, and measure outcomes on cluster members.

Four aspects of the CRT design deserve special attention. First, as the main outcome of interest is community transmission, clusters should be defined as entire municipalities or regions rather than individual schools. Larger clusters have the advantage of minimizing the likelihood of people moving in and out during

the study. Furthermore, this approach best approximates how school reopening will be implemented outside of any randomized evaluation, where all schools within any given region would be expected to reopen at approximately the same time.

Second, clusters should be randomized and intervened upon simultaneously. Infectious disease outbreaks have strong temporal trends. As a result, a stepped wedge design, in which the intervention is rolled out to clusters at different times, has a high risk of bias and is not recommended in these circumstances.[30] A parallel arm design protects against temporal biases.

Third, interventions to be compared are two policies: continued school closure and partial reopening of schools operating under precautions, including social distancing, protective equipment, and disinfection procedures. Interventions will need to be flexible, allowing schools to implement procedures as they would outside of the research setting. Flexibility may encourage both recruitment and retention of clusters as well as enhance the applicability of the results. A second-phase design might additionally consider a comparison of a partial reopening under precautions with fully reopened schools operating largely on pre-pandemic models, for example, without social distancing thereby allowing schools to operate at full capacity.

Finally, since what policymakers need to know most in the context of school closures is whether there is any increased harm from reopening, this lends itself to a non-inferiority design. Alternatively, as we propose, the study should be sufficiently large to render resulting confidence intervals around effects narrow enough to allow interpretation fully without reliance on statistical significance. Whatever approach is taken, interpretation of study findings would require consideration of the level of increased incidence rates that would be deemed acceptably small to be outweighed by the benefits of schools reopening.

Timing

CRTs intended to generate data about the impact of school reopening should be conducted only when relevant policymakers are already planning to reopen schools in all municipalities and regions to be included in the study. This approach will entail learning from government decisions that would be taken even in the absence of research, while minimizing the imposition of risk exclusively for research purposes—an important consideration when consent is not possible, as discussed below.

Reopening should only be considered when community transmission is under control. Control may be defined in terms of the virus' basic reproduction number (typically $R0 < 1$) or a sustained decline in incident cases below a set threshold. As reopening schools may result in increased community transmission, policymakers will need to ensure that the public health system has capacity for contact tracing, isolation, and testing of symptomatic and exposed people. Furthermore, the health system should have the capacity to deal with an increase in COVID-19 cases. Where these conditions are not yet met, precautionary approaches to school closures remain most appropriate from an epidemiologic perspective, although we acknowledge that from educational and economic perspectives, precautionary approaches may favor school reopening.

Resources

The exact trial design and sample size will depend on setting and the prevalence of infection circulating in the community. Given the variability of infection rates by region, measuring this as part of a baseline survey and restricting randomization will help maximize the likelihood that the control and intervention arms of the study are balanced and might be used to inform sample size calculations. Illustrative sample size calculations are included in the supplemental material and suggest somewhere between 50 and 150 municipal or regional clusters and around 1500–3000 viral tests per cluster repeated just prior to randomization to reopening and again 4–8 weeks later. Efficient and realistic scenarios involve between 300,000 and 450,000 polymerase chain reaction or serology tests, such that conducting this type of CRT will demand substantial investment from the government. These calculations also reveal that there is considerable sensitivity in power to within-cluster correlations and prevalence of the outcome. Baseline surveys can therefore additionally inform resources required to ensure the trial delivers precise estimates of effects. The size of the sample required almost certainly necessitates a large budget, but given the economic impact of school closures, this is likely reasonable and consistent with other responses to public health emergencies.[31]

Ethical considerations

Beyond these scientific design considerations, CRTs also raise complex ethical and regulatory issues. In contrast to guidelines specific to individually randomized trials, the *Ottawa Statement for the Ethical Design and Conduct of CRTs* provides guidance for researchers and research ethics committees specific to CRTs.[32] Here, we consider four ethical issues: minimization of risks, protection for vulnerable participants, involvement of gatekeepers, and informed consent.

Minimization of risks

Conducting CRTs only when relevant policymakers previously decided to close schools in all relevant municipalities and regions and are now planning to reopen them has an important impact on how we understand the research risks attributable to the trial, as opposed to background conditions.

In the proposed CRTs, clusters would be randomized to partial reopening with precautions (study intervention) or continued school closure (control). In regions assigned to partial reopening, schools would have partially reopened in the absence of the trial, such that there are no incremental infection risks attributable to the research. In clusters assigned to the control condition, the consequence of research participation would be prolonged closure of schools that would have otherwise partially reopened. As this is likely the safest condition with respect to SARS-CoV-2 transmission, CRT participation does not increase infection risks for participating schools, municipalities, or regions relative to the government partially reopening all relevant schools independent of the study. Accordingly, in terms of potential impact on community transmission, the proposed CRTs are at minimal risk.

However, there are still burdens to consider, particularly for parents and children in clusters randomized to control conditions and therefore stopped from planned reopening. Parents may have to arrange and pay for caregivers or further delay returning to work, while children will be burdened by being unable to socialize with friends and experiencing further educational delay. While these burdens require careful attention, they are a continuation of the burdens already experienced in daily life during the pandemic. Therefore, even though they are different from what would be experienced by study participants absent the research in settings where schools would otherwise move to reopening, they may reasonably be regarded as posing minimal risk, especially given widespread variability in school reopening and closure decisions, even across relatively similar communities. As is true in other contexts involving the minimal risk standard, however, we acknowledge that this assessment is likely to be a matter of some debate. It will be critical to keep the CRTs as short in duration as possible to answer the research question. In addition, further steps can be taken by policymakers to minimize the impact of these burdens, including funding to offset economic burdens, as well as resources for remote learning and interventions to make up lost instructional time when schools reopen. Where governments already have burden-reduction measures in place, the continuation of these measures in the control arm of the trial should not be considered a research-related cost.

Vulnerable participants

Some children, including those from disadvantaged families and areas, will be vulnerable to heightened risks if their schools remain closed, such that relevant supports to minimize those risks should be provided. These might include measures already undertaken in some localities such as opening schools exclusively for the most vulnerable students or increased home learning contact, in addition to other remote social supports, including access to free meals. For schools randomized to partially reopen, children who have medical conditions that place them at higher risk should be allowed to continue remote learning or to do so if this is simply the parents' preference. School staff who are older or who have medical conditions that place them at higher risk also should be given the option of working from home for the duration of the study.

Gatekeepers

To achieve adequate enrolment and avoid loss of clusters after randomization and attrition bias, school districts and schools must be ready and willing to participate in both of the randomized conditions. Feasibility, therefore, demands that relevant school officials provide permission for the enrolment of their schools in the CRT, which should entail consulting with parents. School officials must further confirm that there are adequate plans and resources in place to protect the safety of students and staff in all randomized conditions.

Because trial participation will impact the entire municipality or region given the focus on community spread, permission of political leaders responsible for promoting the interests of their constituents must also be obtained.[33] These gatekeepers should be expected to ensure that adequate resources are in place where SARS-CoV-2 transmission rates increase during the CRT.

Informed consent

International ethics guidelines articulate a general requirement to obtain informed consent from or on behalf of research participants,[32,34] which here would include school children, teachers, and staff, as well as members of the wider community. Yet, as is the case with many CRTs evaluating public health policies, conducting the trial with informed consent would be infeasible. Individuals cannot control whether their schools reopen (beyond the political process) and all members of participating communities stand to be affected. This is why it matters whether the risks of research

participation are minimal, as discussed above. When that condition is satisfied, international guidelines allow for a waiver of consent with approval from a research ethics committee, the idea being that the benefits of allowing research to proceed outweigh remaining individual considerations. The waiver of consent should not extend, however, to data collection procedures, including all research-related polymerase chain reaction or serology testing, for which informed consent feasibly could be secured.

Conclusion

As cases and deaths from COVID-19 ebb and flow in countries around the world, the question of when and how to de-implement public health policies is pressing. In addition, many regions are facing new waves of outbreaks—and new lockdowns. Whether and when schools can reopen (and remain open) will continue to be a question of upmost importance throughout this pandemic. At present, policymakers are left to make such decisions in the absence of rigorous evidence. CRTs can help change that but will demand substantial collaboration, funding, and commitment to generate the level of certainty required.

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Supplemental material

Supplemental material for this article is available online.

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